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Crystal Meth and HIV/AIDS: A Pilot Study of Behavioral and Clinical Correlates

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Abstract

Crystal methamphetamine is an extremely addictive stimulant that increases sexual arousal while reducing inhibition and judgment. Its use is associated with a range of high-risk sexual behaviors that increase the likelihood of acquiring or transmitting HIV. Given the relatively high prevalence of crystal methamphetamine use among people living with HIV and among men who have sex with men, there is great concern that this drug is fueling the HIV epidemic. Equally worrisome are the effects that crystal methamphetamine use can have on the prognosis and overall health of HIV-infected patients. This article reports the results of a pilot study that is part of a larger project exploring the correlates of antiretroviral therapy drug resistance.

Keywords: HIV, latency-reversing therapeutics, concept analysis, HIV, stigma

Introduction

Known by various street names (most commonly, “ice” and “glass”), crystal methamphetamine (CM) can be smoked, snorted, injected, swallowed, or inserted into the rectum. Compared with other illegal drugs, CM is inexpensive, readily available, and provides a stronger, longer-lasting “high” (8–24 hours). Prevalence of use in the U.S. is difficult to pinpoint, but estimates of past-year use from national cross-sectional surveys range from 1.5% to 2.8% among young adults [1].

Commonly cited reasons for using CM, aside from peer pressure, are increased sexual sensitization, mood enhancement, and disinhibition. However, the drug is also used to provide an escape from stress, depression, alienation, and loneliness, all of which are common among people living with HIV [2]. Furthermore, many HIV-infected people report using CM as a way to deal with their illness or with homophobia or prejudice. Consequently, CM use is highly prevalent among people living with HIV. In a San Francisco study, 19% to 39% of HIV-infected people reported using CM during the previous year. This high prevalence is alarming because CM use can increase the risk for HIV transmission and also contribute to poorer health outcomes in HIV-infected users [3, 4].

Methamphetamine Use and HIV Transmission

CM use increases the risk for HIV transmission and acquisition in several ways. First, the drug lowers sexual inhibitions, impairs judgment, and provides the necessary energy and confidence to engage in sexual activity for prolonged periods of time. As a result, methamphetamine users are more likely than nonusers to engage in unprotected anal sex and to have sex with injection drug users, HIV-positive partners, and those of unknown HIV status; they also tend to report a greater number of sex partners and to have a history of other sexually transmitted diseases (STDs) [5].

Second, CM use is a well-documented cause of erectile dysfunction, which can lead users to engage in even higher-risk sexual activities. For example, users who cannot sustain an erection may switch to receptive anal sex (“bottoming”), which carries a higher risk of HIV acquisition than does insertive anal sex. Alternatively, users may take erectile-dysfunction drugs, and the combination of these with CM can lead to longer, more-aggressive periods of sex, potentially resulting in condom breaks or mucosal tears, which can cause bleeding and increased risk of HIV transmission [6, 7].

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Third, CM causes mucosal dryness, which increases the risk for tissue tears. Additional damage to rectal tissues can occur when CM is inserted into the rectum ("keistering," "booty bumping").

Finally, when CM is injected, needle sharing can greatly enhance transmission of HIV and hepatitis viruses [8]. Crystal methamphetamine-using seropositive individuals are at greater risk for ARV drug resistance, a relationship that is attributable to one or more of three causal mechanisms, of which two are clinical and one is behavioral.

Cellular suicide. Crystal methamphetamine use stimulates the secretion of tumor necrosis factor (TNF), a cytokine whose levels are already high in HIV-positive individuals. High levels of TNF trigger a biochemical pathway that leads to cellular suicide, a condition known as apoptosis. In HIV-positive people, crystal methamphetamine boosts TNF levels, which can induce CD₄ apoptosis. This facilitates increased viral replication and thus reduced ARV effectiveness [9].

Metabolism rates. Crystal methamphetamine can alter ARV drug absorption and breakdown, expediting elimination of ARV drugs via metabolic pathways as a result of drug-drug interactions. Accelerated metabolism of ARV drugs lowers bloodstream levels to below the threshold required to manage the virus. This can increase viral loads, prompting the onset of resistance [10]. Indeed, this is precisely what a recent San Diego study found: crystal methamphetamine-using seropositive individuals on highly active antiretroviral therapy (HAART) experienced higher viral loads than those on therapy who either had never tried crystal methamphetamine or who had been clean for at least 30 days [11].

Adherence. There is a behavioral link between crystal methamphetamine and ARV drug resistance through methamphetamine's association with inadequate adherence to dosing schedules. In other words, crystal methamphetamine use can impair adherence. Sporadic adherence contributes to ineffective inhibition of viral replication and thus the onset of ARV drug resistance [12]. In addition to compromised HAART effectiveness, the HIV-crystal methamphetamine nexus may also produce potentially fatal effects. In the human body, CYP2D6 is a liver enzyme that metabolizes both methamphetamines and protease inhibitors (PIs). Some PIs -- especially ritonavir (RTV) and delavirdine (DLV) -- have a greater affinity for this enzyme than do methamphetamines [13, 14, 15]. When taken together, CYP2D6 will metabolize the PI before it will metabolize crystal methamphetamine. Delayed metabolizing of crystal methamphetamine allows levels in the bloodstream to rise to dangerous levels, especially in the brain -- a 3-to 10-fold increase -- which can result in fatal overdose [16].

Methamphetamine Use and Progression of HIV Disease
In addition to facilitating HIV transmission, CM use is associated with detrimental behavior changes that can affect the prognosis and overall health of people living with HIV. For instance, current methamphetamine use decreases adherence to HIV treatment and medical follow-up.¹⁰ Frequent CM use has also been associated with increased

risk for antiretroviral resistance [17] particularly to NNRTIs, with the obvious implications for treatment and transmission risk. For example, CM use is thought to have contributed to the acquisition of triple-class-resistant virus by the New York City patient described in 2005 [18]. In addition, some patients use CM to treat HIV-associated symptoms, such as fatigue, instead of seeing a physician. Such self-medication may lead to underdiagnosis and undertreatment of HIV and to important complications such as anemia and hypogonadism [19].

CM use may also influence progression and complications of HIV disease more directly. For example, animal studies have shown that CM can impair the immune system and increase HIV replication, and human studies suggests that it can accelerate the progress of HIV-related dementia.

Other Consequences of Methamphetamine Use

Other consequences of CM use that are particularly harmful to HIV-infected patients include deterioration of the teeth and gums (a result of dry mouth and grinding of the teeth), reduced appetite, poor eating habits, and weight loss. Furthermore, many users "crash" after using CM for several days straight and are left with little energy and the very feelings they were trying to avoid — depression and isolation [20].

Other adverse effects of CM use include intense cravings for CM when not taking it; tachyphylaxis; increased risk for heart attack and stroke (because of increases in blood pressure, heart rate, and body temperature); impaired memory, reasoning, and ability to process information; and psychological problems, such as depression, psychosis, aggressive behavior, hallucinations, and paranoia. Chronic use can also cause skin lesions and damage the cardiovascular system, lungs, liver, muscles, and nerve cells in the brain.

Although methamphetamine is not known to affect HIV medications, some PIs increase absorption and decrease metabolism of CM, leading to severe reactions or overdosing [21].

Preventing and Treating Methamphetamine Addiction

Prevention of methamphetamine use is hampered by a relative paucity of epidemiologic data that would enable us to assess the magnitude of the current problem adequately and to evaluate the efficacy of various interventions. Despite federal efforts to restrict pseudoepinephrine imports and a nationwide decline in small methamphetamine laboratories, the drug continues to be widely available. A report from the National Drug Intelligence Center suggests that Mexican drug traders have relocated their labs from the U.S. to Mexico and have expanded distribution to the midwestern and eastern U.S., underscoring the difficulties of drug enforcement in the era of global trade. Developing methamphetamine prevention "task forces" (involving community members and representatives from at-risk groups, STD treatment centers, health departments, and law enforcement) is a reasonable approach, despite a lack of efficacy data [22]. Educational campaigns should be tailored to specific target populations, and care should be taken to help ensure that such campaigns do not increase cravings in CM-addicted patients.

Given the high prevalence and dire consequences of CM use among HIV-infected patients, clinicians should be sure

to ask patients about past or current use. Drug testing is recommended for all patients who have a history of, or are suspected of, using CM.

Few data are available to recommend any one method of methamphetamine treatment over another. Cognitive behavior-based interventions (Matrix Model), 12-step programs, drug testing, and contingency management interventions have been used by different treatment centers, with varying degrees of success. Nevertheless, treatment of CM addiction can be successful in decreasing risky sexual behaviors and should be an integral part of any HIV prevention effort [23].

Method

Participants in the present study comprise a purposive sample of randomly chosen 22 physicians. Physicians were asked to complete a 45-item questionnaire that contained a series of questions pertaining to their HIV-positive patients. Questions were clustered into five themes:

- physician's practice and patient profile;
- medication, adherence, resistance;
- illicit drug use;
- psychiatric symptoms; and
- Sexual activity.

Two-tailed, Pearson's product-moment correlations were computed across items for behavioral and clinical cofactors. Because analyses were conducted on a small, purposive sample, results should be interpreted as indicating trends that signal the need for further investigation.

Statistical analysis

Participants were divided into the following 3 categories depending on their history of drug use: (1) those who reported methamphetamine use in the past 90 days; (2) those who reported no hard drug use in the past 90 days, including those with no history of drug use and those who may have used hard drugs but not in the past 90 days; and (3) those who reported the use of other hard drugs (excluding methamphetamine) in the past 90 days. Hard drug use was defined as the use of at least 1 of the following drugs in the past 90 days: cocaine, crack, hallucinogens, injection drugs, flunitrazepam (Rohypnol; Hoffman-La Roche, Basel, Switzerland), γ -hydroxybutyric acid, 3, 4-methylenedioxymethamphetamine (ecstasy), or other drugs (excluding marijuana).

To assess the association of methamphetamine, use with HIV sexual risk behavior, regression models were fit to the data using generalized estimating equations to control for possible correlation in the data among participants enrolled at the same venues. In addition, the models controlled for possible confounding by age and race/ethnicity. $P < .05$ was considered statistically significant.

Results

Physician Practice and Patient Profile

On average, 60% of physician-members' patients are HIV-infected; 55% are gay men. Five percent of the physicians see one to five HIV-positive patients per week; 21% see six to 10 per week; 29% see 11 to 20 per week; 24% see 21 to 50 per week; and 21% see more than 50 HIV-positive patients per week. Seventy-six percent of HIV-positive patients are on HAART. Forty-five percent of the patients

are on an RTV-containing regimen, 3% on a DLV-containing regimen. At the time of the survey, 55% had undetectable viral loads, 20% were resistant to just one ARV drug, and 30% to multiple ARV drugs. Fifty-two percent of patients self-report to their physicians that they have missed taking their medications in the past month. The number increases to 70% for the past six months. Most patients cite reasons such as "forgot" and "traveling" for the missed doses. The second and third most common reasons for missing doses include physical side effects and the disruptive nature of controlled substances, respectively. Physicians report extensive and varied illicit drug use by their patients. Crystal methamphetamine was the most commonly ingested drug for 11% of the patients. Forty-six percent of these patients reported using another controlled substance beside crystal methamphetamine. Of this group, 62% most commonly ingested alcohol, 21% most commonly ingested cocaine, 12% an erectile dysfunction medication, and 11% marijuana. The sixth most commonly ingested drug was ecstasy, followed by gamma hydroxybutyrate (GHB) and ketamine, respectively. The physicians indicated that they believe 23% of their patients are habitual users of one or more controlled substances. Eleven percent of patients self-report taking an ARV "drug holiday" specifically because of illicit drug use. Only one third of the patients were described as "very well informed" about the relationship between drugs and HIV.

Patients reported to their physicians a variety of socio-sexual behaviors. Fifteen percent of patients used Internet-based services to arrange sex, 13% had visited a bathhouse, and 8% had attended a circuit party. Eleven percent of patients self-report insertive unprotected anal intercourse (UAI) in the past six months; 8% report receptive UAI. Twenty-one percent of those who reported any type of UAI said they were using crystal methamphetamine at the time the UAI occurred. Another 32% of patients were high on another substance, and 53% of patients had consumed alcohol prior to or during the sexual encounter. Physicians believe that slightly more patients are "very well informed" about the relationship between drugs and sex (43%) than are very well informed about the relationship between such drugs and HIV (33%).

Crystal Methamphetamine and Resistance: Behavioral Risk Factors

Crystal methamphetamine use at one point in time increases the likelihood of future use. Crystal methamphetamine use in the past week is positively correlated with use in the past month ($r = 0.975$, $P < 0.001$), use in the past three to six months ($r = 0.833$, $P < 0.001$), and use in the past 12 months ($r = 0.908$, $P < 0.001$). The use of crystal methamphetamine is associated with a series of risk factors connected to ARV drug resistance. For example, those who report crystal methamphetamine as their most commonly ingested drug within the past month show a trend for missing a medication dose in the past month ($r = 0.417$, $P < 0.085$). Crystal methamphetamine users also participate in high-risk lifestyles. Those who used crystal methamphetamine in the past week, month, or 12 months were more likely to have gone to a bathhouse ($r = 0.387$, 0.374, and 0.422, respectively; $P < 0.05$) and circuit party ($r = 0.667$, 0.657, 0.613, respectively; $P < 0.001$). Crystal methamphetamine use is also connected to incidences of UAI. Those who used crystal methamphetamine in the past

week, past month, and past 12 months were more likely to engage in insertive UAI ($r = 0.662, 0.626, 0.541, P < 0.001$) and receptive UAI ($r = 0.792, 0.729, 0.640, P < 0.001$), two high-probability HIV transmission-related sexual behaviors.

Crystal Methamphetamine and Resistance: Clinical Risk Factors

The survey instrument did not solicit specific information on TNF, metabolism, or CYP2D6. Results on the clinical aspect of the crystal methamphetamine/resistance relationship are therefore limited. Results do, however, suggest that those who used crystal methamphetamine in the past three to six months were also likely to be on an RTV-containing regimen ($r = 0.335, P < 0.028$), which exacerbates the likelihood of a fatal drug-drug interaction. Those patients who self-report crystal methamphetamine as their most commonly ingested drug show a trend for being resistant to multiple ARV drugs ($r = 0.446, P < 0.083$). The most substantively noteworthy finding, however, is that crystal methamphetamine use in the past week, month, three to six months, or 12 months is not correlated with having an undetectable viral load ($r = 0.014, P < 0.939; r = 0.071, P < 0.697; r = -0.001, P < 0.995$; and $r = -0.028, P < 0.879$, respectively). If the counterfactual is true, then those who do not report crystal methamphetamine use are likely to be those for whom HAART is effective and vice versa.

Discussion

Results reveal that clinical and behavioral pathways undergird the relationship between crystal methamphetamine use and ARV drug resistance. The still-nascent literature emphasizes the role of inadequate adherence as a critical behavioral factor responsible for resistance. Study results are confirmatory. The possibilities for addiction are in place as patients who report using crystal methamphetamine at one point in time are also likely to report future use. Addiction concerns aside, crystal methamphetamine users are more likely to engage in a number of HIV-transmittable sexual behaviors such as insertive and receptive UAI. These findings are especially troubling because crystal methamphetamine users are more likely to visit bathhouses and attend circuit parties, where there may be an overall high prevalence of seropositive patrons and riskier sexual practices. The public health threat is exacerbated given that: (1) seropositive individuals exhibit a less cautious sexual profile, (2) crystal methamphetamine-using seropositive individuals are less likely to be adherent to their ARV regimen (which then increases the likelihood of ARV drug resistance), and (3) crystal methamphetamine-using seropositive individuals on HAART are likely to have higher viral loads.

Study results corroborate the role played by behavioral and clinical factors in the relationship between crystal methamphetamine and ARV drug resistance. Although instrument limitations precluded testing for the direct or indirect role played by ARV drug metabolism, neurological damage, or apoptosis, results did reveal that those individuals who reported using crystal methamphetamine in a variety of different time periods were not likely to have undetectable viral loads. If the reverse is also true (i.e., that those who do not use crystal methamphetamine are statistically more likely to have undetectable viral loads),

then there is further evidence for a clinical relationship between crystal methamphetamine use and ARV drug resistance. Much more research is required into this important and growing area of public health concern.

Conclusion

To date, little research has examined how crystal meth use influences HIV medical outcomes among HIV-infected "men have sex with men" (MSM). This analysis showed a significant independent association between crystal meth use and unsuppressed viral load among MSM in an HIV service population. Future studies should examine biological and psychosocial mediators, moderators and confounders of this relationship to inform intervention development for MSM crystal meth users in HIV care settings

Conflict of Interests

This paper does not contain any conflict of interest.

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